PATENT
Docket No. 300622000113

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Marian Christopher

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Chaitan KHOSLA, et al.

Serial No.: Continuation of 09/263,184

Filing Date: August 8, 2001

For: RECOMBINANT PRODUCTION OF NOVEL POLYKETIDES

Examiner: Nashaat T. Nashed, Ph.D.

Group Art Unit: 1652

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination of the above-referenced application, the Examiner is respectfully requested to enter the following amendments. Enclosed in the following Exhibit A:

Exhibit A: Marked-up Version of Amendments to the Specification.

sd-51777

AMENDMENTS

In the Specification:

Please amend paragraph one of the specification as follows:

--This application is a continuation of U.S. Patent Application Serial No. 09/263,184, filed May 3, 1999, which is a continuation-in-part of U.S. Patent Application Serial No. 08/164,301, filed December 8, 1993, which is a continuation-in-part of U.S. Application Serial No. 08/123,732, filed September 20, 1993, from which priority is claimed pursuant to 35 U.S.C. §120, and which disclosures are hereby incorporated by reference in their entireties.--

In the Claims:

Please cancel Claim 1 and insert claims 96 to 115:

96. A method to prepare a cell containing at least one nucleic acid molecule, wherein said molecule comprises at least one module that encodes a modular polyketide synthase (PKS) functional in catalyzing the synthesis of a polyketide, said module comprising at least one nucleotide sequence which encodes a PKS acyl transferase (AT) activity; at least one nucleotide sequence which encodes a PKS ketoacyl carrier protein synthase (KS) activity; and at least one nucleotide sequence which encodes a PKS acyl carrier protein (ACP) activity;

said module operatively linked to a control sequence, whereby a functional modular PKS is produced in said cell, with the proviso that said module or said control sequence is heterologous to the host cell;

said method comprising introducing said nucleic acid molecule into a host cell.

97. The method of claim 96 wherein said introduced nucleic acid molecule and optionally additional nucleic acid molecules comprise a complete modular PKS gene cluster.

98. The method of claim 96 wherein said host cell has been modified so as completely to lack a PKS gene cluster normally present in the unmodified said host cell.

99. The method of claim 98 wherein said host cell is *S. coelicolor*.

100. The method of claim 96 wherein said module comprises:
at least one nucleotide sequence encoding PKS ketoreductase (KR) activity; or

at least one nucleotide sequence encoding PKS ketoreductase (KR) activity and
at least one nucleotide sequence encoding PKS dehydratase (DH) activity; or

at least one nucleotide sequence encoding PKS ketoreductase (KR) activity and
at least one nucleotide sequence encoding PKS dehydratase (DH) activity, and
at least one nucleotide sequence encoding PKS enoyl reductase (ER) activity; and

optionally,
at least one nucleotide sequence encoding PKS thioesterase (TE) activity.

101. The method of claim 100 wherein said module comprises:
at least one nucleotide sequence encoding PKS ketoreductase (KR) activity and
at least one nucleotide sequence encoding PKS dehydratase (DH) activity; and
at least one nucleotide sequence encoding PKS enoyl reductase (ER) activity.

102. The method of claim 96 wherein said module is a 6-deoxyerythronolide B synthase module.

103. The method of claim 96 wherein said nucleic acid molecule and optionally additional nucleic acid molecules comprise the complete 6-deoxyerythronolide B synthase gene cluster.

104. A method to produce a functional polyketide synthase which method comprises culturing cells prepared by the method of claim 96 under conditions wherein said module is expressed.

105. A method to produce a functional polyketide synthase which method comprises culturing cells prepared by the method of claim 97 under conditions wherein said module is expressed.

106. A method to produce a functional polyketide synthase which method comprises culturing cells prepared by the method of claim 102 under conditions wherein said module is expressed.

107. A method to produce a polyketide which method comprises culturing cells prepared by the method of claim 96 under conditions wherein said module is expressed to produce functional PKS protein so as to produce said polyketide.

108. A method to produce a polyketide which method comprises culturing cells prepared by the method of claim 97 under conditions wherein said module is expressed to produce functional PKS protein so as to produce said polyketide.

109. A method to produce a polyketide which method comprises culturing cells prepared by the method of claim 102 under conditions wherein said module is expressed to produce functional PKS protein so as to produce said polyketide.

110. The method of claim 96 wherein the host cell is an Actinomycete.

111. The method of claim 110 wherein the host cell is a *Streptomyces*.

112. The method of claim 111 wherein the host cell is *S. coelicolor* or *S. lividans*.

113. The method of claim 104 wherein said cells are Actinomycetes.

114. The method of claim 113 wherein said cells are *Streptomyces*.

115. The method of claim 114 wherein said cells are *S. coelicolor* or *S. lividans*.

REMARKS

The present application is a continuation of U.S. Serial No. 09/263,184 which is currently pending. Originally filed claims 1 through 95 are cancelled. New claims 96 to 115 are currently pending. The present claims are supported by the claims as originally filed as well as by the entire application. An example of such support is pages 4 through 7 of the specification. The specification has been amended to provide additional priority information. No new matter has been added and entry of the amendment is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no.300622000113. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: August 8, 2001

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EXHIBIT A. VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

This application is a continuation of U.S. Patent Application Serial No. 09/263,184, filed May 3, 1999, which [This application] is a continuation-in-part of U.S. Patent Application Serial No. 08/164,301, filed December 8, 1993, which is a continuation-in-part of U.S. Application Serial No. 08/123,732, filed September 20, 1993, from which priority is claimed pursuant to 35 U.S.C. §120, and which disclosures are hereby incorporated by reference in their entireties.